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BOSTON -- Scientists for the first time have identified a fault in the brain waves of schizophrenics that may explain their hallucinations and disturbed thinking. The study, by a team at the Veterans Affairs (VA) Boston Healthcare System and Harvard Medical School, appears in the Nov. 8 *Proceedings of the National Academy of Sciences*.

The researchers studied the brain waves of normal and schizophrenic patients as they responded to images. Those with the disorder showed no electrical activity in a certain frequency—the “gamma” range, from 30 to 100 brain waves per second—that healthy brain cells use to exchange information about the environment and form mental impressions. “The schizophrenics did not show this gamma-band response at all. There was a pretty dramatic difference,” said senior author Robert W. McCarley, MD, deputy chief of staff for mental health services at the VA Boston Healthcare System and chair of the Harvard psychiatry.

The brain contains hundreds of billions of neurons, or nerve cells. Researchers believe our thoughts are created when large groupings of these neurons “fire”—send messages to each other, through bursts of electrical activity—at the same frequency. Different frequencies, measured in hertz, or cycles per second, indicate different levels and types of activities. Delta waves, below 4 hertz, occur during sleep. Alpha waves, 8 to 13 hertz, occur at relaxed, quiet times. Beta waves are the next fastest, occurring when we are actively thinking.

Gamma waves are harder for scientists to detect because of their low amplitude. But McCarley, lead author Kevin M. Spencer, PhD, and colleagues used a method that checks for synchronicity of the wave cycle—that is, high and low points that line up—to capture gamma activity. Successive waves “in phase” mean brain cells are communicating.

The team used electroencephalogram (EEG) to record the brain waves of 20 schizophrenic and 20 normal patients as they looked at either of two images containing “Pac-man” figures. In one image, the four shapes were arranged to optically suggest a square in the center. The participants had to press a button to show if they perceived the square or not.

Both groups were able to respond within a second, but those with schizophrenia made more errors and took about 200 milliseconds longer to process the images. More significantly, they showed no evidence of gamma activity “phase-locked” to the pressing of the button, which would have indicated that the brain was normally processing the visual perception guiding their response.

“What some of them did show was a response at a lower frequency, outside the gamma band, which may indicate less efficient communication among neurons,” said McCarley. “If the most efficient communication between assemblies of neurons is at 40 hertz, and the schizophrenics are using a lower frequency, it’s likely they have defective communication between cell assemblies and brain regions.” He added that the strongest non-gamma activity was shown by patients with the worst schizophrenia symptoms.

Schizophrenia affects about one percent of the population, or 2.2 million Americans. It is the most common psychotic illness, and accounts for some 40 percent of VA’s mental health costs. Contrary to popular notion, it does not involve a “split personality”; that is a rare and separate condition. The disease does involve delusions, in which patients may think others are plotting against them; hallucinations, where they hear voices or see figures that aren’t real; and disorganized thinking and behavior, where they may have trouble conversing or focusing on a task.

Antipsychotic medications help many patients control symptoms, but often have unwanted side effects. McCarley said drugs that promote a normal gamma response among neurons would likely help the condition. His VA-Harvard group is exploring which receptors in the brain are involved. “If you know the neurochemical identity of the neurons and synapses involved in generating gamma activity, you can try to target treatments toward them,” he said.

The study was supported by grants from the Department of Veterans Affairs and the National Institute of Mental Health, and a grant to Spencer from the National Alliance for Research on Schizophrenia and Depression. Spencer is also a VA Research Enhancement Award Fellow.

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